Analyzing more protein samples with the same headcount: Is open access LC/MS part of a solution for increasing throughput while decreasing analysis turnaround time?

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OVERVIEW

- Biopharmaceutical companies are increasing sample throughput demands on their analytical groups without a commensurate increase in analyst headcount.
- Analyst time has become a limited commodity, and many R&D groups experience delays of days to weeks for simple intact mass characterization of their molecules.
- Open access LC/MS provides a mechanism for organizations to leverage one analytical scientist to enable one or multiple research groups to carry out routine LC/MS analysis, with minimal or limited analyst involvement.
- In this poster, characteristics of an Open Access environment are explored. A system configured analysis of intact and reduced antibodies (heavy/light chain) is presented as a prototype application of open access for the biopharmaceutical environment.

BEST PRACTICES FOR EMPLOYING OPEN ACCESS LC/MS

Open Access LC/MS has found widespread acceptance within small molecule pharmaceutical development organizations. Successful deployments within large molecule environments will likely favor a very similar set of environmental and analysis characteristics:

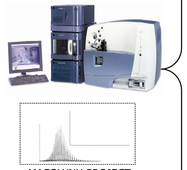
1) Organizational desire to simplify user interactions with LC/MS instruments, or empower one analyst to more efficiently support groups of non-LC/MS experts.
2) Organizational need for more structured and automated processes for data and result management.
3) Systems are dedicated for a common class of analyte and analysis. A system used for Open Access protein and peptide LC/MS would not routinely be used for nucleic acid SEC/MS or glycan HILIC/MS analyses.
4) Analyses are routine or predictable, and users can be provided a reasonable number of robust and generic standard methods to choose from.
5) Standard approaches to data processing and result reporting can be employed.
6) Users are sufficiently trained and capable of preparing samples for LC/MS analysis.

RELATIONSHIP BETWEEN THE SYSTEM ADMINISTRTOR, SYSTEMS AND USERS

Administrator:
- Configures system
- Daily care and feeding
- Creates analysis, data processing & report methods
- Remote system monitoring

Users:
- Enter name and sample info
- Select from method list
- Place samples where indicated
- Can receive e-mailed results and interactive OpenLynx reports

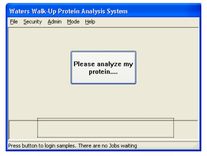
FILE AND REPORT MANAGEMENT



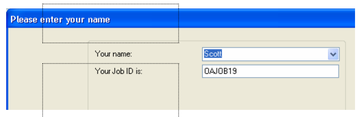
- Store raw data in a generic MassLynx project
- Store raw data in a user-specific MassLynx project
- Copy MassLynx projects to a generic or user-specific local or network locations (post-acquisition)
- Copy/Move raw data to generic or user-specific local or network locations (post-acquisition)
- Protection from data loss
- Automation of data archiving
- Providing users raw data access

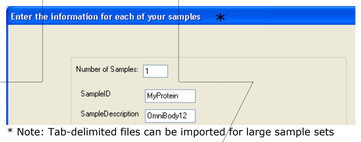
- E-mail .RPT file to User
- E-mail .RPT file to Administrator
- Store .RPT file in up to 3 generic local/network locations
- Copy/Move .RPT file to user specific local/network location
- Print report to PDF file and store in generic location
- E-mail PDF to user
- E-mail PDF to Administrator
- Export for other programs (e.g. database, bioinformatics, LIMS) as txt, tab, csv or xml
- Store in generic or user location

USER EXPERIENCE IN A "WALK-UP" OPEN ACCESS ENVIRONMENT

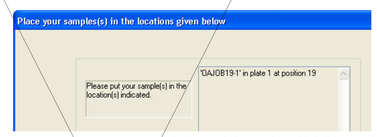


SAMPLE LOGIN SCREEN

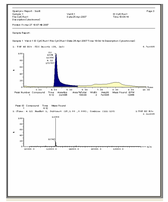


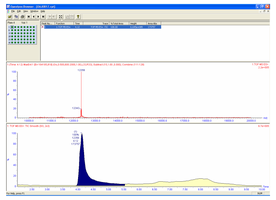


* Note: Tab-delimited files can be imported for large sample sets

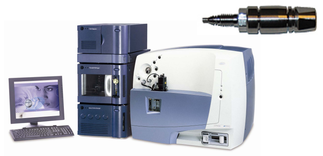


Printed Results (PDF) and OpenLynx .RPT file can be e-mailed to user.
(.RPT are viewable/interactive within the OpenLynx browser)

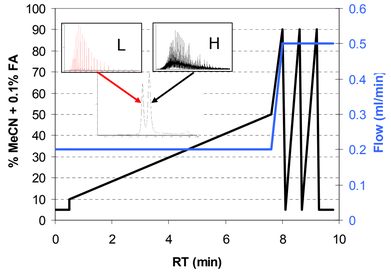




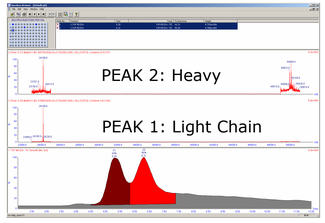
OPEN ACCESS FOR REDUCED ANTIBODIES



The combination of rapid LC separations (for concentration and desalting of antibody samples) and high mass accuracy ESI-TOF MS detection represents a robust open access LC/MS configuration for the analysis of intact and reduced IgG's. System configuration: Acquity UPLC, MassPrep Micro desalting Column (2.1 x 5 mm), LCT Premier ESI-TOF MS.

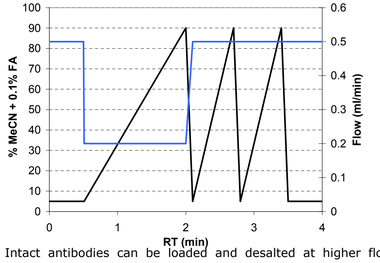


An robust method for Open Access LC/MS should deal with a range of sample matrices (buffers, salts, etc.) and restore the system to pre-injection conditions after each analysis. The method (above) for generic analysis of heavy and light chains starts with an isocratic hold at initial conditions, with a post-column diversion valve sending salts and other nonvolatiles to waste. A series of sawtooth gradients eliminates the need for blank runs between difficult samples.

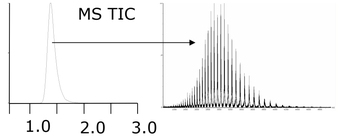


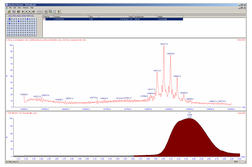
OpenLynx Browser view of a reduced antibody Open Access LC/MS run. Deconvoluted spectra were automatically generated by combining scans under each of the detected peaks, and applying MaxEnt1 spectral deconvolution over two targeted mass ranges.

OPEN ACCESS FOR INTACT ANTIBODIES

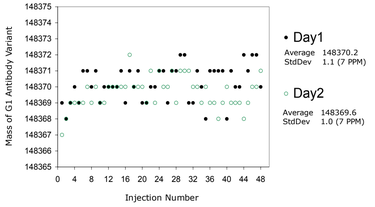


Intact antibodies can be loaded and desalted at higher flow rates than reduced subunits without detectable breakthrough. A more aggressive gradient can be applied, as protein desalting rather than chromatographic subunit resolution is the primary goal of the online method.





Representative Total Ion Chromatogram (TIC, Top Left), summed raw spectrum, and OpenLynx processed deconvoluted spectrum for an intact IgG1.



The mass stability of the modern TOF mass spectrometer produces consistent results over large sets of samples. In this example, a 48 vial IgG1 sample set was submitted for Open Access LC/MS over two consecutive days. The G1F/G0F variant mass was plotted from each run.

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